

What is claimed is:

SUB A' 1. A compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding hormone-sensitive lipase, wherein said compound specifically hybridizes with and 5 inhibits the expression of hormone-sensitive lipase.

SUB B' 2. The compound of claim 1 which is an antisense oligonucleotide.

3. The compound of claim 2 wherein the antisense oligonucleotide has a sequence comprising SEQ ID NO: 62, 70, 10 99, 107, 108, 111, 112, 115, 117, 121, 123, 124, 132, 133, 142, 146, 153 or 179.

4. The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.

15 5. The compound of claim 4 wherein the modified internucleoside linkage is a phosphorothioate linkage.

SUB B' 6. The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified sugar moiety.

7. The compound of claim 6 wherein the modified sugar 20 moiety is a 2'-O-methoxyethyl sugar moiety.

8. The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified nucleobase.

9. The compound of claim 8 wherein the modified nucleobase is a 5-methylcytosine.

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10. The compound of claim 2 wherein the antisense oligonucleotide is a chimeric oligonucleotide.

SUB A2
A2

11. A compound 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecule encoding hormone-sensitive lipase.

12. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier or diluent.

13. The composition of claim 12 further comprising a colloidal dispersion system.

14. The composition of claim 12 wherein the compound is an antisense oligonucleotide.

15. A method of inhibiting the expression of hormone-sensitive lipase in cells or tissues comprising contacting said cells or tissues with the compound of claim 1 so that expression of hormone-sensitive lipase is inhibited.

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16. A method of treating an animal having or suspected of having a disease or condition associated with hormone-sensitive lipase comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1 so that expression of hormone-sensitive lipase is inhibited.

17. The method of claim 16 wherein the animal is a human.

18. The method of claim 16 wherein the condition is an abnormal metabolic condition.

19. The method of claim 18 wherein the metabolic condition is hyperlipidemia.

20. The method of claim 16 wherein the disease is diabetes.

5 21. The method of claim 20 wherein the diabetes is Type 2 diabetes.

22. The method of claim 16 wherein the condition is obesity.

23. The method of claim 16 wherein the condition is a
10 hyperproliferative disorder.

24. The method of claim 23 wherein the hyperproliferative disorder is cancer.

25. The method of claim 24 wherein the cancer is
15 pituitary, colorectal, breast, testicular, pulmonary or epithelial cancer.

26. A method of modulating blood glucose levels in an animal comprising administering to said animal the compound of claim 1.

27. The method of claim 26 wherein the animal is a human.

20 28. The method of claim 26 wherein the blood glucose levels are plasma glucose levels.

29. The method of claim 26 wherein the blood glucose levels are serum glucose levels.

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30. The method of claim 26 wherein the animal is a diabetic animal.

31. A method of preventing or delaying the onset of a disease or condition associated with hormone-sensitive lipase in an animal comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1.

32. The method of claim 31 wherein the animal is a human.

10 33. The method of claim 31 wherein the condition is an
abnormal metabolic condition.

34. The method of claim 33 wherein the metabolic condition is hyperlipidemia.

35. The method of claim 31 wherein the disease is
15 diabetes.

36. The method of claim 35 wherein the diabetes is Type 2 diabetes.

37. The method of claim 31 wherein the condition is obesity.

20 38. The method of claim 31 wherein the condition is
a hyperproliferative disorder.

39. The method of claim 38 wherein the hyperproliferative disorder is cancer.

40. The method of claim 39 wherein the cancer is pituitary, colorectal, breast, testicular, pulmonary or epithelial cancer.

41. A method of preventing or delaying the onset of an
5 increase in blood glucose levels in an animal comprising
administering to said animal the compound of claim 1.

42. The method of claim 41 wherein the animal is a human.

43. The method of claim 41 wherein the condition is an
10 abnormal metabolic condition.

44. The method of claim 43 wherein the abnormal metabolic condition is hyperlipidemia.

45. The method of claim 41 wherein the disease is diabetes.

15 46. The method of claim 45 wherein the diabetes is Type
2 diabetes.

47. The method of claim 41 wherein the condition is obesity.

48. The method of claim 41 wherein the condition is
20 a hyperproliferative disorder.

49. The method of claim 48 wherein the hyperproliferative disorder is cancer.

50. The method of claim 49 wherein the cancer is
pituitary, colorectal, breast, testicular, pulmonary or
25 epithelial cancer.

51. A method of modulating serum cholesterol levels in an animal comprising administering to said animal the compound of claim 1.

52. The method of claim 51 wherein the animal is a human.

53. The method of claim 51 wherein the condition is an abnormal metabolic condition.

54. The method of claim 53 wherein the abnormal metabolic condition is hyperlipidemia.

55. The method of claim 51 wherein the disease is diabetes.

56. The method of claim 55 wherein the diabetes is Type 2 diabetes.

57. The method of claim 51 wherein the condition is obesity.

58. The method of claim 51 wherein the condition is a hyperproliferative disorder.

59. The method of claim 58 wherein the hyperproliferative disorder is cancer.

60. The method of claim 59 wherein the cancer is pituitary, colorectal, breast, testicular, pulmonary or epithelial cancer.

61. A method of modulating serum triglyceride levels in an animal comprising administering to said animal the compound of claim 1.

62. The method of claim 61 wherein the animal is a human.

63. The method of claim 61 wherein the condition is an abnormal metabolic condition.

5 64. The method of claim 63 wherein the abnormal
metabolic condition is hyperlipidemia.

65. The method of claim 61 wherein the disease is diabetes.

66. The method of claim 65 wherein the diabetes is Type
10 2 diabetes.

67. The method of claim ~~61~~ wherein the condition is obesity.

68. The method of claim 61 wherein the condition is a hyperproliferative disorder.

15 69. The method of claim 68 wherein the
hyperproliferative disorder is cancer.

70. The method of claim 69 wherein the cancer is pituitary, colorectal, breast, testicular, pulmonary or epithelial cancer.

20 71. The compound of claim 1, wherein said compound specifically hybridizes with and inhibits the expression of a nucleic acid molecule encoding an alternatively spliced form of hormone-sensitive lipase.